REMARKS

Receipt of the Office Action mailed December 2, 2005 is acknowledged. New claim 30 has been added. Support for new claim 30 can be found throughout the original disclosure, for example, at page 17, line 10. Upon entry of the amendment, claims 21, 22, 24, 25 and 30 will be pending in the application. No new matter is believed to be entered.

35 U.S.C. Section 103 Rejections

Claim 21 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Cusack et al. (U.S. Patent No. 5,302,348) in view of Mintz (U.S. Patent No. 4,551,308) and further in view of Shepherd et al. (WO 94/08237). Reconsideration and withdrawal of the rejection are respectfully requested. The Examiner takes the position that Cusack et al. disclose the claimed invention with the exception of an agglutinating reagent, scanning the 10% portion of liquid sample at 540 nm or detecting the amount of scattered radiation to avoid hemolysis interference.[1] However, the Examiner concludes that it would have been obvious at the time of the invention to modify Cusack et al. to provide these features in view of the teachings of the secondary references of Mintz and Shepherd et al. Applicants submit that for the reasons set forth below, the skilled artisan would not have been motivated to modify Cusack et al. Furthermore, even if Cusack et al. were so modified, the combined teachings still would not suggest the claimed invention.

For the purpose of determining the strength of an agglutination reaction in the present application, an agglutinating reagent, such as the preferred agent described in the present application at page 17, lines 10-17 is used in conjunction with mixing to provide rapid coagulation of the sample as an enabler for the subsequent

[1] Applicants note that neither the 540 nm nor the scattered radiation claim features are present in independent claim 21.

determination of the strength of agglutination reaction (which can be used to determine blood type) by spectroscopic means.

As the Examiner correctly notes, Cusack et al. fail to teach or suggest an agglutinating reagent. Instead, Cusack et al.'s device is designed to determine the coagulation rate of whole blood irrespective of whether the blood is unaltered (unmedicated) or has been subjected to heparin (an anti-coagulant) or a combination of heparin and protamine (an anti-coagulant and heparin neutralizer). In particular, the device is used to establish the baseline coagulation rate of a patient's blood before surgery. During surgery, to prevent complications due to blood coagulation, heparin is administered to significantly extend the time required for the patient's blood to coagulate. Cusack et al.'s device can be used to verify this extended time to coagulate and, hence, confirm that the proper dose of heparin has been administered. At the conclusion of the surgery, protamine is administered to restore the baseline level of coagulation by neutralizing the effect of the administered heparin. Again Cusack et al.'s device can be used to confirm that the proper dose of protamine has been administered and that a patient's baseline coagulation time has been restored.

The computation of the proper doses of heparin and protamine are performed outside the domain of the Cusack et al.'s device using such parameters, *inter alia*, as the strength of the heparin reagent, the strength of the protamine reagent, and the weight of the patient. It should be noted, as indicated by Cusack (see, column 1, line 37 et. seq. and column 1, line 55 et. seq.) that both heparin and protamine vary greatly in strength, which greatly complicates the accurate computation of dosage. Also the weight of the patient is an instrumental variable used as an uncertain substitute for the patient's blood volume, which is not directly measurable. Because of these uncertainties, a reagent, e.g., heparin, is administered and Cusack et al.'s device is then used to measure the impact on blood coagulation. In a trail-and-error fashion, this process continues until the patient's blood coagulation time is long enough for the surgery. The reverse happens at the end of surgery for the dosage of protamine. Cusack et al. clearly teach both heparin and protamine are ***anti-coagulants*** (see Cusack column 1, line 37 and column 2, line 4).

Mintz's device is an attempt to remove some of the uncertainty surrounding the heparin or protamine dosage computation by observing the impact of a series of heparin or protamine concentrations on the coagulation time of the patient's blood. This removes some of the uncertainty regarding the strength of the heparin or protamine, but not the patient's blood volume. However, as with Cusack et al. the only reagents used in Mintz's device are either heparin or protamine, ***both of which are anti-coagulants*** (see Cusack column 1, line 37 and column 2, line 4). Therefore, to describe Mintz's reagents as coagulation (agglutinating) agents is incorrect. In fact, they would be better described as anti-coagulation (or anti-agglutinating) agents. Thus, Mintz fails to teach an agglutinating reagent as claimed.

Moreover, one skilled in the art would have been motivated away from combining the teachings of Mintz and Cusack et al. Specifically, the introduction of Mintz's reagents in any combination (except stoichiometric equivalents which would have no impact) would slow down the coagulation process rendering the test procedure of Cusack et al. less efficient. Hence, one skilled in the art would have been motivated away from using Mintz's reagents in Cusack et al.'s device.

In addition, the method taught by Cusack et al. and the claimed method are fundamentally different. That is, agglutination in Cusack et al. is determined by **timing fluid flow**. See e.g., Cusack et al. at column 5, lines 1-10,

> As the blood passes the narrowed region, the blood begins to coagulate and clot along the roughened surface of the narrowed region, eventually occluding the **normal flow** through the narrowed region. When the **traversed time** of **one cycle of travel** is a predetermined percentage longer than an immediately preceding cycle of travel, **coagulation is considered to have occurred** and the over all time for coagulation is displayed to the operator.

(emphasis added). The photoelectric sensors of Cusack et al. are utilized to detect the passing of a fluid front as part of a means to **measure fluid flow rate**. Once the fluid front has been detected, there is no more meaningful information gathered by the photoelectric sensors (i.e., these are utilized in a binary fashion rather than an analog fashion).

In contrast, determining the strength of an agglutination reaction in the claimed invention is determined by detecting the **amount** of light absorbed or scattered with a beam of light (claim 21, step d), and the calculating the amount of agglutination from the absorbance of scattering (claim 21, step g). Thus, in the claimed invention, agglutination is determined by measuring the amount of absorbance, not by measuring fluid flow rates as is done in Cusack et al.

The Examiner applies Shepherd et al. as teaching the use of a predetermined wavelength to minimize the error criterion in absorbance and detecting the amount of scattered radiation to avoid any hemolysis interference. However, since Cusack et al. only use photodetectors to detect the presence of blood to start the timing cycle (see, e.g., column 9, line 67 to column 10, line 10), the skilled artisan would have had no motivation to go to the added trouble of including a predetermined wavelength or detecting the amount of scattered radiation.

Moreover, Shepherd et al. is fundamentally different from the present invention. Shepherd et al. teach an analysis methodology that employs a series of measurements all at differing wavelengths on unaltered whole blood with a goal of determining the fraction or percentage of a plurality of different species, e.g., total hemoglobin concentration, and the concentrations of the following pigments of interest: bilirubin, oxy-, deoxy-, carboxy-, met-, and sulfhemoglobin. The process and goal of the claimed invention is significantly different in that it teaches an analysis methodology that employs a series of measurements in time (i.e., step f, claim 21) at certain predetermined wavelengths on blood that has been treated with an agglutination reagent. One of the useful results attainable with the present invention is in determining blood type, i.e., A, B, AB, or O, of the sample. The blood sample in the Shepherd teaching is essentially static and unchanging over the measurement time horizon whereas the sample (e.g., blood) in the present invention has been treated with an agglutinating reagent that reacts over the measurement time horizon with the sample. The rate at which this reaction takes place is dependent upon the specific pharmadynamics of the sample and agglutinating reagent.

For example, in the preferred embodiment of blood as the sample, the rate of reaction will depend on the blood type of the red blood cells in the sample reacting with the agglutinating reagent. Under a constant set of analysis conditions, measurement data on blood samples of A, B, AB, and O would be processed and manipulated to generate a family of four related, but different discrete set of (time, % agglutination) ordered pairs of measurements. Smooth curves could then be drawn through these four sets of data to yield a family of four curves representing the reaction progression for each of the blood types as a function of time. Since these curves tend to diverge at greater values of time finding the % agglutination at a fixed point in time is sufficient to identify the blood type of the sample (see the present application at page 19, line 30 et. seq.).

The methodology taught in Shepherd et al. to compensate for light scatter during the measurements is directed at the analysis of **unaltered, whole blood**. In contrast, in the claimed method, compensating for light scatter during the measurements is directed at partially agglutinated sample, in particular the partially or wholly supernatant portion of the sample, which is significantly different from the unaltered whole blood taught by Shepherd et al.

Claim 22 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Cusack et al. (U.S. Patent No. 5,302,348) in view of Mintz (U.S. Patent No. 4,551,308) and further in view of Shepherd et al. (WO 94/08237) and further in view of Zabetakis et al. (U.S. Patent No. 5,773,305) in view of Cusack et al. (U.S. Patent No. 5,302,348). Reconsideration and withdrawal of the rejection are respectfully requested. The Examiner takes the position that Zabetakis et al. teach the claimed invention except for scanning of the sample at predetermined wavelength or an agglutinating reagent within the first cavity.

Applicants submit that claim 22 is patentable over the combination of Cusack et al., Mintz, Shepherd et al. and Zabetakis et al. for the reasons set forth above with respect to claim 21.

Furthermore, the teaching of Zabetakis is that of providing a means to achieve a homogenous mix of fluids rather than moving fluids in a fashion gentle

enough to promote and detect agglutination reactions, many of which can be quite fragile and are easily destroyed by fluid shear forces. Thus there would have been no motivation to combine the teaching of Cusack et al., Mintz, Shepherd et al. and Zabetakis et al. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The examination of these claims and passage to allowance are respectfully requested. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (732) 524-1496 to clarify any unresolved issues raised by this response.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Account No. 10-0750/CDS0255/TJB. This sheet is submitted in triplicate.

Respectfully submitted,

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DATED: March 1, 2006